

Amendments to the Specification:

Please replace title with the following amended title:

~~ANTIBODIES TO NON-FUNCTIONAL P2X₇ RECEPTOR DIAGNOSIS AND TREATMENT
OF CANCERS AND OTHER CONDITIONS~~

Please replace paragraph [0006] with the following amended paragraph:

[0006] The amino acid sequences of the human and rat P2X₇ receptors are known, for example, from US patent. No. 6,133,434 (Buell et al). Refer also to ~~FIG. 1 herein~~ (SEQ ID NO:1[D]).

Please replace paragraph [0020] with the following amended paragraph:

[0020] In the case of human P2X₇ receptors, the specific sequence involved in the conformational change may include Pro210, which undergoes a change in conformation from the trans form to the cis form in the absence of bound ATP. Thus, in the case of human receptors, an appropriate epitope sequence against which an antibody must be raised may include Pro210, and may extend either side of this residue, to an appropriate extent necessary to induce an antibody response. By way of non-limiting example, this may include a segment extending from Gly200 to Thr215 or Gly200 to Cys216. Further, a homologous segment (i.e., cognate segment) from other mammals, such as rat, may be used where this cross-reacts with human tissue. Allelic variants of the sequence shown in ~~FIG. 1~~ SEQ ID NO:1 can also be used. As an example, the same segment Gly200 to Cys216 in rat may be used, although there are two amino acid substitutions in the rat sequence compared with the human sequence (refer U.S. Pat. No. 6,133,434, for example). Therefore, the segment used to generate antibodies is preferably a polypeptide comprising a segment including or consisting of Gly200 to Thr 215 or Gly200 to Cys216. Preferably, the segment includes no more than 30 contiguous amino acids from a P2X₇ receptor, and more preferably consists of Gly200 to Thr215 or Gly200 to Cys216.

Please DELETE paragraph [0074] and the text on page 16, lines 4-7:

~~BRIEF DESCRIPTION OF THE DRAWING~~

~~[0074] Figure 1 (SEQ ID NO:1) shows the amino acid sequence of the human P2X₇ receptor (prior art). Sequences 65 to 81 and 200 to 216 are highlighted and are referred to below.~~

Please replace paragraphs [0084-0085] with the following amended paragraphs:

[0084] To raise the antibody specifically to non-functional P2X₇, the epitope used was the sequence 200 to 216 in **Figure 1 SEQ ID NO:1**, containing a Cys at 216.

[0085] To raise the antibody to non-discriminatory P2X₇, the epitope used was the sequence 65 to 81 in **Figure 1 SEQ ID NO:1**, to which was added an N-terminal Cys. This antibody could not detect whether the receptor was non-functional but was designed to detect all receptor so that the proportion of receptor that was functional could be determined by comparing the staining obtained by using the two antibodies separately.

Please replace paragraphs [0095-0096] with the following amended paragraphs:

[0095] In these experiments, the adjuvant used was the ~~QAIGEN~~ QIAGENTM Pty Ltd product, ~~ImmunEasy~~TM IMMUNEASYTM which contains the immuno-stimulatory product CpG DNA, (trademark of ~~Coley Pharmaceutical Group Inc.~~)

[0096] 5 µg of epitope or conjugated epitope was diluted in 70 µL of PBS and 30 µL of ~~ImmunEasy~~TM IMMUNEASYTM adjuvant. Mice were injected at multiple sites subcutaneously and intramuscularly. This regime was repeated two weeks later and again at a further two weeks. Mice were bled eight days after the third injection. Antibodies raised in mice by this method were again able to discriminate between the different P2X₇ epitopes and the antibodies against the P2X₇ non-functional epitope gave the same results as those raised in sheep and rabbits.

Please replace paragraph [0125] with the following amended paragraph:

[0125] It is believed that application to patients in general would involve production of a human monoclonal antibody (such as ~~hereceptin~~ HERCEPTINTM) so that internal cancers could

be treated with the same efficacy as is revealed with topical application. All normal functional P2X₇ expressed on the cell surfaces of cells such as lymphocytes would need to remain unaffected by the presence of the antibody to avoid side effects. The antibody should therefore only bind to proteins expressed on the cell surface of cells attempting to but unable to initiate apoptosis. Thus all cells targeted would be only those attempting to kill themselves through programmed cell death, including cancer cells. The P2X₇ receptors on these cells, particularly cancer cells, would be in a non-functional or ATP-depleted state.